IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No.	: 10/758,415
Applicant	: William S. Brusilow
Filed	:January 16, 2004
TC/A.U.	: 1614
Examiner	: Zohreh Vakili
Docket No.	: 2930-109
Customer No.	: 06449
Confirmation No.	: 5654

PRE-APPEAL BRIEF REQUEST FOR REVIEW

Mail Stop AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

August 5, 2008

Dear Commissioner:

Applicants request review of the final rejection (Office Action of May 5, 2008) in the above-identified patent application. In the Office Action, claims 1-5 and 21 were finally rejected under 35 USC §102(b) as being anticipated by Apostolakis or Ginefri-Gayet and claims 10-11 were finally rejected under 35 USC §102(b) as being anticipated by Liedtke. A request for reconsideration in response to the Office Action dated November 6, 2008, which included the same rejections, was filed on February 5, 2008. A review of these rejections is requested for the following reasons.

Claims 1-5 were rejected under 35 USC §102(b) as anticipated by Apostolakis or Ginefri-Gayet. Applicants respectfully point out that Apostolakis discloses that MSO is a centrally acting neurotoxin with convulsive properties. The office action dated May 5, 2008 indicates on page 3 that the examiner does not agree with this statement. Applicants point out the first sentence on page 257 of Apostolakis

which states that that "[M]ethionine sulfoximine (MSO) is a centrally acting neurotoxin with convulsive properties; it has been used for a long time as a tool for the experimental study of epilepsy (20)". Apostolakis also teaches that MSO can cause deformation, atrophy, loss of striation of muscle fibers, fibrosis and degeneration of Purkinje cells in the cerebellum. Apostolakis concludes that administration of MSO to rabbits in addition to the known convulsive effects may also be responsible for hind leg myopathy. The MSO dosage used by Apostolakis was 3-8 mg/kg body weight. Apostolakis does not suggest or disclose that MSO can be used to treat polyglutamine diseases such as Huntington's disease, spinocerebellar ataxia, and spinobulbar muscular atrophy and in view of the undesirable side effects discussed in Apostolakis (i.e. deformation, atrophy, loss of striation of muscle fibers, fibrosis and degeneration of Purkinje cells in the cerebellum) one skilled in the art would not be motivated to administer MSO to patients with a polyglutamine disease.

Ginefri-Gayet discloses that MSO, when administered at a convulsant dose (100-200 mg/kg body weight administered intraperitonealy or 50-75 µg per rat administered by ICV injection) induces a decrease in body temperature. Ginefri-Gayet indicates that MSO elicited a time dependent regional perturbation of 5-HT metabolism which could be due to the marked rise in ammonia levels caused by the irreversible inhibition of the activity of glutamine synthetase. Ginefri-Gayet suggests that the 5-HT receptor plays a role in MSO elicited hypothermia in the rat. Ginefri-Gayet does not suggest or disclose that MSO can be used to treat polyglutamine diseases such as Huntington's disease, spinocerebellar ataxia, or spinobulbar muscular atrophy and in

view of the undesirable side effect (hypothermia), one skilled in the art would not be motivated to treat patients with polyglutamine diseases with MSO in view of the disclosure in Ginefri-Gayet.

The applicant respectfully points out that the present claims are directed to a method for treating a polyglutamine disease which is not disclosed or suggested by either Apostolakis or Ginefri-Gayet. The composition and kit claims were withdrawn from consideration in view of applicant's election of group I for examination in the present application. Though Apostolakis indicates that MSO suppresses the formation of glutamine and glutamate, Apostolakis also states that "[M]ethionine sulfoximine (MSO) is a centrally acting neurotoxin with convulsive properties" (page 257, left column) and that "[F]ollowing the IV MSO administration, the animals became hyperactive and exhibited increased hind leg muscle tonus at 2 hr; at 4-5 hr tetanus-like seizures started..." (page 259, left column). Apostolakis also states in the paragraph bridging pages 260-261 that "[I]n conclusion, administration of small does of MSO to rabbits except for their already known convulsive effects, may also be responsible for hind leg myopathy (rigid paralysis with histological findings resembling myositis)". Ginefri-Gayet indicates that MSO is a convulsant molecule that induces a decrease in body temperature (page 173, left column). Ginefri-Gayet states on page 178, right column that "[I]njection of MSO into the third ventricle, allowing the drug to interact more directly not only with thermoregulatory centers in the hypothalamus but also with brainstem and midbrain neuronal structures, led to a rapid decrease of body temperature, reaching its maximum value during the course of the 0200-0230 h period

following administration of MSO". Thus, Ginefri-Gayet discloses that MSO elicits hypothermia at a dose of 50-75 µg/ 10 µl. In view of the numerous undesired effects caused by MSO (hypothermia, convulsant, neurotoxin) discussed in the cited prior art, applicants contend that not only does the cited prior art fail to anticipate the presently claimed method for treating a polyglutamine disease, but the cited prior art teaches away from administering MSO to any patients for therapeutic purposes. Therefore, applicants request that the examiner's decision be reversed.

Claims 10 and 11 were rejected under 35 USC §102(b) as anticipated by Liedtke et al. Liedtke discloses an ion channel which is involved in osmoregulation and mechanoreception in vertebrates. The only mention of MSO in Liedtke is in paragraph 207 which discusses mammalian expression vectors such as a glutamine synthetase/ methionine sulfoximine co-amplification vector such as pEE14. There is no suggestion or disclosure regarding the administration of MSO for treating a polyglutamine disease. Since claims 10 and 11 depend directly or indirectly from claim 1 which recites a method for treating a polyglutamine disease, applicants request that the examiner's decision be reversed and this rejection be withdrawn.

For the reasons set forth above, Applicants respectfully request review of the final Office Action, and submit that all pending claims are patentable. In the event this paper is not considered to be timely filed, the Applicant respectfully petitions for an appropriate extension of time. Any fee for such an extension together with any additional fees that may be due with respect to this paper, may be charged to Counsel's Deposit Account No. 02-2135.

Respectfully submitted,

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